

TREATMENT OF STANDARDIZED FRACTURES BY EXTRACORPOREAL SHOCKWAVE THERAPY (ESWT)

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Abstract- ESWT is used in treatment of pseudoarthrosis and may be considered for callus lengthening operations. In this study, effects of ESWT on the forming callus were studied. Transverse femoral osteotomy at mid diaphysis, internally fixated with Kirschner wires were performed on 20 male, ten-week-old white Wistar rats. In the third week, animals underwent ESWT with 1500 (Group I) and 500 (Group II) shockwaves/treatment at a generating voltage of 10 kV on their right femurs; left femurs were used as controls. In the ninth week animals were sacrificed. X-Ray and computerized tomographical analyses on both femurs were done. X-Ray data showed that bone tissue of Group I displayed a higher percentage of nonunions and secondary axial displacements than Group II. Group II had a higher percentage of unions and fewer secondary axial displacements than Group I. The radiological scores for 500-sw/treatment group were 67% of the controls. CT data showed that ESW treated right legs in both groups had a greater callus area, and lower average density of image pixel than controls. In agreement with other studies done on healing bone, no significant correlation between callus area and the level of bone healing was found.

Keywords - Bone, femur, rat, callus, X-Ray, CT.

I. INTRODUCTION

Extracorporeal Shock Wave Therapy (ESWT) makes use of shock waves, which are produced by electrohydraulic, electromagnetic and piezoelectric means and focused on the body by use of concave reflectors. Studies on the effects of shock waves on living tissues, blood vessels, nerves, renal tissue [1] and bony structures [7], show that it produces a cavitation effect on the exposed tissue, leading to hemorrhage [14], making it suitable for use in cholelithiasis, prostate carcinoma and melanomas [4,7,18,19]. Having an analgesic effect, shock waves, are also used in treatment of tendinosis calcarea, tennis elbow and heel spurs [6,11,15]. Another application area for ESWT is pseudoarthrosis [9,12,13]. In bone tissue, ESWT imitates a fresh fracture leading to bone formation. The mechanism of healing by ESWT may be similar to that of surgery, where the cartilaginous link between the bones is re-injured mechanically by means of a scalpel or other instruments, providing an effect similar to that of a fresh fracture.

Microscopic examination of bones display small ruptures and bleeding in bone trabeculae, similar to a fresh fracture. After ESW treatment, a fast rate of bone formation, corresponding to an increase in the number of osteoblasts is observed [6]. However, there is still controversy on the treatment dosage, the number of shocks per treatment, as well as the possible mechanisms of stimulation of osteogenesis.

Our study aimed to answer these questions and provide data for fracture treatment using ESWT. We wanted to challenge the questions of dosage, mechanism and timing of ESW application by (a) administering two different amounts of shock waves generated at the same voltage and (b) applying shock waves on the forming callus, on day 20, at the end of inflammation period, and examining their effect on healing.

II. METHODOLOGY

Osteotomies were carried out at the Experimental Animals Laboratory of Istanbul University, Cerrahpasa Medical School. 20 male, 10 week-old, white Wistar rats, weighing from 131 gr. to 160 gr. were used. Animals were anesthetized by intramuscular injections of 3 mg/kg of xylazine hydrochloride (Rompun 23.32 mg/ml, Bayer Turk, Istanbul, Turkey) and 10 mg/kg of ketamine hydrochloride (Ketalar, 50 mg/ml, Eczacibasi, Istanbul, Turkey). A 2 cm incision was made over the femur and the muscles were reflected. Using a mini-saw, a transverse defect was created in the midshaft of the femur. The periosteum was preserved and a 1.0 mm thick Kirschner wire was inserted through the medullary canal, extending proximally and distally. After the operation, as a prophylactic antibiotic, 10 mg/kg Cefazolin (Bilim ilaç, Istanbul, Turkey) was administered intramuscularly. No complications occurred during and after the operation and all of the 20 animals survived without infections. Animals were not immobilized after the operation.

At the end of the third week, animals were randomized into two groups of ten each and were anesthetized using the above-mentioned amounts of xylazine hydrochloride and ketamine hydrochloride. The right femurs of animals in the first group were exposed to 1500 shockwaves/treatment at a

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generating voltage of 10 kV using a hydraulic lithotripter (PCK Medical Systems, Stonelith-Litho3pter, Ankara, Türkiye). Shockwaves were focused on the osteotomies radiologically, using a biplanar intersecting X-Ray system with image intensifier chain and a television monitor for target imaging. In order to attain perfect coupling, ultrasound gel was used and target location was rechecked several times during the course of treatment. The untreated left femurs were used as controls. The right femurs of animals in the second group were exposed to 500 shockwaves/treatment at a generating voltage of 10 kV. The untreated left femur were used as controls. One animal from each group did not receive ESW treatment due to diarrhea and high tolerance to anesthetics respectively.

After the ESW treatment, animals were not immobilized. During the course of the experiment, four animals from the first group and two animals from the second group died due to diarrhea. The remaining five animals from the first group and the seven animals from the second group survived till the termination of the experiment.

The experiment was terminated at the end of the ninth week, forty four days after ESW treatment, by ether sacrifice of animals. Bones were excised, muscle and soft tissues were removed, with only the callus remaining. Femur were fixed in 10% formalin solution for five hours and then preserved in a 50% ethanol solution in centrifuge tubes.

Topographic X-Ray films of bones were taken and used to determine the stage of bone healing, which was quantified by scoring on the healing parameters using a system modified by Ref [1]. Radiological scoring on early, middle and late phases of bone healing was carried out by three independent examiners, who were blind to the experiment. Scoring of the observers on periosteal reaction, quality of union, and bone remodeling were summed and averaged. These averages were analyzed using Student's t-test to find significance of results between and within the groups.

Callus area was quantified by Computerized Tomography, (CT) (Siemens, Somatom AR Star). Contiguous 1.0 mm high resolution CT slices were taken from proximal to distal at a slice thickness of 1.0 mm. Measurements were carried out throughout the medullary canal. The periphery of callus was drawn manually, giving us both the callus area in mm² and the average density of image pixel in Hounsfield units. Callus area and average density of image pixel analyses between and within groups were performed using Student's t-test.

III. RESULTS

A. Figures and Tables

The ultimate criterion of bone healing is the presence of a union. Results of macroscopic and radiological examination of bone union are listed in Table I, II and III.

TABLE I
MACROSCOPIC AND RADIOLOGICAL EXAMINATION OF LEFT AND RIGHT FEMUR

Group	Union	Nonunion
I (1500 sw)	1 Right, 2 Left	4 Right, 3 Left
II (500 sw)	5 Right, 7 Left	2 Right

TABLE II
RADIOLOGIC SCORING OF FEMUR TREATED WITH 1500 SHOCKWAVES (GROUP I)

Animal/ Femur	Periosteal Reaction	Quality of Union	Bone Remodelling	Total Score
1 / Right	0	0	0	0
1 / Left	0.67	1.33	0.67	2.67
2 / Right	0	0	0	0
2 / Left	2	0.67	0	2.67
3 / Right	1.33	0	0	1.33
3 / Left	1	0	0	1
4 / Right	0	0	0	0
4 / Left	2	1.67	0.67	4.34
5 / Right	3	3	2.33	8.33
5 / Left	3	3	2.33	8.33

TABLE III
RADIOLOGIC SCORING OF FEMUR TREATED WITH 500 SHOCKWAVES (GROUP II)

Animal/ Femur	Periosteal Reaction	Quality of Union	Bone Remodelling	Total Score
1 / Right	3	3	1.67	7.67
1 / Left	2.33	2.33	0.67	5.67
2 / Right	2.67	1.67	0.67	5
2 / Left	2.67	2.67	2	7.3
3 / Right	3	3	1.67	7.67
3 / Left	3	2.33	0.67	6
4 / Right	1	0	0	1
4 / Left	3	3	1.33	7.33
5 / Right	1	0	0	1
5 / Left	3	3	1.33	7.33
6 / Right	3	2.33	0.67	6
6 / Left	3	2.67	1.33	7
7 / Right	2.67	2	0.67	5.33
7 / Left	3	3	1.33	7.33

Callus size and properties were examined using high resolution CT, giving minimum and maximum average density of image pixel and callus area in mm² listed in Table IV.

TABLE IV
CALLUS DENSITY AND AREA BY CT ANALYSIS

	Min. and Max. Average Density of Image Pixel	Total Callus Area (mm ²)
Group I - right femur	-170 to 400	5.72
Group I - left femur	122 to 560	6.6
Group II - right femur	-80 to 158	1.34
Group II - left femur	-153 to 168	0.57

IV. DISCUSSION

In assessment of the effectiveness of any method used to enhance fracture healing, the ultimate criterion is the presence of a union. At the time of termination of this study, on the 64th day of osteotomies, theoretically speaking, the femurs would have been in their third stage of bone healing, by when an adequately healing bone would have attained a union. However, radiological analysis indicated that among the bones in Group I there was 30% union in both femurs, and 20% union in the treated femurs, with 57% of the nonunions in the treated femurs. Group II had 85.7% bone union and 71.4% union in the treated femurs. All of the nonunions in

this group were in the treated femurs. Macroscopic and radiological inspection showed that bone healing in Group II was superior to Group I.

It is expected that in an adequately healing bone, in its third healing phase, the total radiological score of 8 or 9 would be attained. Radiological scoring of bone healing, done by orthopaedists blind to the study, showed that healing in Group II (81.29) was again superior to Group I (29). The high number of nonunions in the treated femurs of Group I lowered the score for this group by not only lowering the radiological score for that leg, but also by retarding the healing of the left femur, thus reducing the overall group radiological score. Student's t-test indicates that there is a difference of 10% significance between the treated femurs scores of the groups.

In experimental fracture healing, CT is being used to determine the properties of fracture callus and the state of bone healing. It has been shown that with CT analysis, the detection of the different phases of bone healing is possible and thus making CT assessment of fracture callus superior to conventional X-Ray [8]. Experimentally, ESWT is known to increase callus size [3], which reaches a maximum two weeks after fracture and is considered to be an indicator of the degree of healing. However, it is also known that an abundant callus size may be associated with secondary axial displacement. In addition, callus volume has been shown to be unrelated to bone mechanical properties and healing properties [3].

In CT analysis, the total callus area of Group I (10.34 mm^2) was found to be 5.4 times greater than that of Group II (1.91 mm^2). Similarly, the callus area of the treated femurs in the first group was higher than that of the second group. However, radiological and macroscopic examination of bones indicated superior bone healing in the second group. Therefore, our findings support the findings of Refs. [3], [10], and [17], and indicate that the larger callus size of the first group is due to the higher number of bone nonunions and secondary axial displacements in this group and that the callus size is not an indicator of the degree of bone healing. Using multiple regression analysis, which accounted for the dependence of callus volume on differences in maturation and the density of callus, Ref. [3], have also demonstrated that callus volume is not a significant factor contributing to the mechanical properties of the fracture.

Callus density and the stiffness of bone increase linearly with calcium content, till about 6 weeks after osteotomy [3]. In CT analyses, average density - mean value of all the pixels within region of interest (ROI) - is given in the Hounsfield unit scale, with values ranging from 0 (air) to 4095. In callus density measurements, the average density of image pixel is expected to increase with increasing mineralization. Knowing that the bones in the second group are at a more advanced stage of healing and mineralization, it was expected to have a higher mineral density in the callus of the second group. However, the average density of image pixel of the second group was lower than the first, varying between -170 and 560

for Group I and between -153 and 168 for Group II. The smallness of area of ROI in the second group, and the resulting sampling site variation, reducing the precision of the measured density, may have caused a lower value of average density of image pixel. Within the groups analysis of callus density indicated expected results: a higher density in the femurs with unions compared to those with nonunions in Group I, and a relatively higher density in the left femurs of the second group when compared to the treated right femurs of this group. Knowing that callus mineralization increases over time to provide the rigidity needed for the remodeling phase of bone healing to start, and that with resorption a lower bone density is observed, we think that lower density of image pixel in the second group is indicative of the more advanced stage of bone healing.

Knowing that the effects of applied dosage are related to the physical properties of experimented animal, i.e. weight, size, femur length, cortical thickness at mid diaphysis, and mineral ash content of the species, the presence of two cases of pseudoarthrosis in the second group may indicate that a treatment using 500 sw / treatment may still be too high for rats of this size and weight. On the other hand, one animal in the first group displayed close to normal healing of both femurs. In terms of height, size and weight, this animal was the largest of both groups.

V. CONCLUSIONS

Statistically insignificant, yet observable and pronounced quantitative differences between the results of the two groups indicate that ESWT applied at the end of the third week at 1500 shockwaves / treatment at 10 kV had a traumatic effect on rat femur, and that ESW application of 500 shockwaves / treatment at 10 kV did not significantly retard healing of bone tissue. ESWT must be administered at low total energy levels. However, the right femur of Group II displayed almost equivalent healing as that of control group. We also confirm the findings of Refs. [10,17], and state that callus size is not an indicator of bone healing in bones treated with ESWT.

Our study did not address the question of the number of treatment sessions to use to administer the total energy. A study relating applied energy, cortical thickness and mineral ash of bone to bone healing would contribute to the development of a ESWT protocol for pseudoarthrosis.

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